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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,542	05/16/2001	Rajesh Manchanda	BERLX-100	9728

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EXAMINER	
WELLS, LAUREN Q	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 04/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/855,542	MANCHANDA, RAJESH	
	Examiner	Art Unit	
	Lauren Q Wells	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-14,16-25 and 27-35* is/are pending in the application.

4a) Of the above claim(s) *7,17,23-25,27-31 and 35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,8-14,16,18-22 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-4, 6-14, 16-25, 27-35 are pending. Claims 7, 17, and 23-25, 27-31 and 35 are withdrawn from consideration, as they are directed to non-elected subject matter. The Amendment filed 8/8/03, amended claims 7, 11, 17, 23, 28.

Deleting the term "prevent" from claim 11 is sufficient to overcome the 35 USC 112, 1st paragraph rejection, in the previous Office Action.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/12/03 has been entered.

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Election/Restrictions

The Examiner maintains the finality of the Election/Restriction requirement. Compositions and kits are distinct inventions. As pointed out in previous Office Actions, the purpose of a kit is to hold something, whereas the purpose of a composition is to combine ingredients to produce an effect. As such, compositions and kits are distinct invention that require divergent searches and that have achieved separate classifications.

Applicant argues that, "applicants arguments traversing the restriction were not addressed in the Final Office Action". This argument is not persuasive. See page 3 of the Final Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6, 8-14, 16, 18-22, 33, 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) Claim 8 and 9 recite the limitations "of claim 5" and "of claim 8", respectively. There is insufficient antecedent basis for these limitations in the claims, as claim 5 has been cancelled.

(ii) The phrase "small organic compound" in claims 1 and 11, found throughout the definition of the formula of the targeting agent, is vague and indefinite, as the metes and bounds of these claims are unascertainable. What are small organic compounds? Are they defined by a certain number of carbon atoms, or a certain configuration, or something else? The specification

does not define this phrase and one of ordinary skill in the art would not be apprised of its meaning.

(iii) Claims 21 and 22 recite the limitations "of claim 15" and "of claim 21", respectively. There is insufficient antecedent basis for these limitations in the claims, as claim 15 has been cancelled.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4, 6, 11, 14, 16, rejected under 35 U.S.C. 102(e) as being anticipated by Russell et al. (2003/0235532).

Russell et al. disclose a sodium iodide symporter genetically fused to either the N-terminus or C-terminus of the product of a transgene through a linker peptide, see abstract. Claim 1on page 9 of Russell et al. discloses administering a nucleic acid comprising the transgene and a sequence encoding a sodium-iodide symporter and labeled iodine. Claim 4 on page 9 of Russell et al. teach the labeled iodine as radioactive iodine. Page 8, section [0150] teaches 124I as one of three preferred radioactive iodines.

Thus, Russell et al. and the instant invention both disclose a radionuclide, a targeting agent, and a compound which releases or generates iodide ions. In Russell et al. the radionuclide

and the compound which releases or generates iodide ions is 124I, and the targeting agent is the transgene with the linker peptide.

It is respectfully pointed out that the linker peptide is a complexing moiety.

While "a method of stabilizing a composition" is not explicitly stated, the Examiner respectfully points out that the above reference teaches the combination of the compound which releases iodide ions to a composition comprising a radionuclide and a targeting agent. Thus, since the same steps are taught for affecting the composition, the method of the above rejection inherently has the property of stabilizing the composition.

Claims 1, 4, 6, 14, 16, are rejected under 35 U.S.C. 102(a) as being anticipated by Thakur (6,395,255).

Thakur teaches a composition for a tumor imaging agent, see abstract. Disclosed is a reagent for radiolabeling a tumor imaging agent comprising 4 amino acids which covalently link a radionuclide to the amino group of each amino acid to form an N4 configuration, wherein N4 configuration is complexed with a tumor specific sequence that enables reagent to bind to a tumor. I-124 is taught as the radionuclide. See Col. 17, lines 38-44 and 51-56. See the examples, beginning in Col. 7, that exemplify the tumor imaging agents in composition.

Thus, Thakur and the instant invention both disclose a radionuclide, a targeting agent, and a compound which releases or generates iodide ions. In Thakur, the radionuclide and the compound which releases or generates iodide ions is I-124, and the targeting agent is the N4 configuration complexed with the tumor specific sequence.

It is respectfully pointed out that the linker peptide is a complexing moiety.

While "a method of stabilizing a composition" is not explicitly stated, the Examiner respectfully points out that the above reference teaches the combination of the compound which releases iodide ions to a composition comprising a radionuclide and a targeting agent. Thus, since the same steps are taught for affecting the composition, the method of the above rejection inherently has the property of stabilizing the composition.

It is respectfully pointed out that the N4 configuration is a complexing moiety.

It is further respectfully pointed out that the N4 configuration comprises 4 amino acids, and that a peptide is defined as comprising two or more amino acids.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 10-14, 16, 20, 33, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. (6,174,513) in view of Banerjee et al. (2002/0151598).

The instant invention is directed toward a composition comprising a radionuclide, iodide ions or a compound which releases/generates iodide ions, and a targeting agent selected from a peptide, oligonucleotide, antibody, peptidomimetic, or the formula of instant claim 1, and method of stabilizing a composition comprising adding the iodide ions or a compound which releases/generates iodide ions to a composition comprising the radionuclide and targeting agent.

Miller et al. teach stabilization of peptides and proteins for radiopharmaceutical use, wherein surfactants in combination with salts are used to stabilize the peptides or proteins.

Technetium-99m and others are taught as suitable radionuclides. The radiolabeled peptide is used with a pharmaceutically acceptable carrier in a method of performing a diagnostic imaging procedure using a scintillation camera. Saline is taught as a pharmaceutically acceptable carrier. The reference lacks compounds that generate/release iodine ions. See Col. 2, lines 11-22; Col. 3, lines 8-Col. 4, line 59; Col. 8, lines 9-42.

Banerjee et al. teach that tonicity adjusting agent can be added to saline solution to provide the desired ionic strength of the pharmaceutical composition. Potassium and sodium iodide are taught as tonicity adjusting agents which display no or only negligible pharmacological activity after in vivo administration. See [0056].

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the potassium iodide, taught by Banerjee et al., to the saline solution of Miller et al. because of the expectation of achieving a composition wherein the tonicity can be adjusted to provide high, medium, or low ionic strength without effecting the pharmacological activity of the active agent.

While "a method of stabilizing a composition" is not explicitly stated, the Examiner respectfully points out that the above rejection teaches adding a compound which releases iodide ions to a composition comprising a radionuclide and a targeting agent. Thus, since the same steps are taught for affecting the composition, the method of the above rejection must have the property of stabilizing the composition.

Claims 18-19, 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miller et al. in view of Banerjee et al. as applied to claims 1-4, 6, 10-14, 16, 20, 33 and 34 above, and further in view of Blum et al. (Chest).

Miller et al. and Banerjee et al. are applied as discussed above. The reference lacks depreotide.

Blum et al. teach 99mTC depreotide as a somatostatin analog as an optimal imaging agent in scintigraphy for solitary pulmonary nodes. This compound is taught as having a great sensitivity for diagnosing malignant or benign pulmonary tumors. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the protein of the combined references as depreotide, as taught by Blum et al., because of the expectation of achieving an imaging agent that is highly sensitive in diagnosing the malignancy of pulmonary tumors and which does not undergo radiolysis (chemical decomposition of the peptide).

Response to Arguments

Applicant argues, "Applicants respectfully disagree that one of ordinary skill in the art would be motivated to modify one pharmaceutical composition by adding elements of any other pharmaceutical composition merely because they are both pharmaceuticals". This argument is not persuasive. The Examiner respectfully points out that Applicant has misconstrued the Examiner's argument in the Advisory Action. Please see the Advisory Action.

Applicant argues, "There is no desirability indicated in the references, i.e., no motivation, for why one of ordinary skill in the art would want to adjust the tonicity of the Miller or Blum compositions by applying the method of Bannerjee". This argument is not persuasive. First, it is respectfully pointed out that Blum is not being modified by Bannerjee, please see the above rejection. Second, it is respectfully pointed out that the above rejection does not apply the method of Bannerjee. Third, as pointed out above, one of skill would be motivated to add the

tonicity adjusting agent of Bannerjee into the composition of Miller because of the expectation of achieving a product wherein the tonicity can be adjusted, wherein such an adjustment is beneficial since the tonicity can be adjusted to the individual needs of patients. It is respectfully pointed out that every composition has tonicity.

Applicant argues, "There is also no teaching in Miller or Blum which would lead one of ordinary skill in the art to believe: 1) that a tonicity adjusting agent would not, in fact, be harmful to the objectives of the Miller or Blum inventions or 2) that a tonicity adjusting agent for bronchodilating compositions would be useful for a radiopharmaceutical composition". This argument is not persuasive. Again, it is respectfully pointed out that Blum is not being modified by Bannerjee, please see the above rejection. Second, it is respectfully pointed out that Banerjee et al. specifically teach potassium and sodium iodide as tonicity adjusting agents which display no or only negligible pharmacological activity after in vivo administration. Third, the Examiner respectfully points out that tonicity adjusting agents are useful for all pharmaceutical compositions that are administered in vivo. The Examiner respectfully points out that tonicity refers to the response of cells or tissues to the solutions in which they are immersed. If cells are placed in a hypertonic solution, net movement of water will be out of the cell, causing the cell to shrivel. If cells are placed in a hypotonic solution, net movement of water will be into the cell, causing the cell to swell or burst. Thus, one skilled in the art would add sufficient solute(s) to the composition so that the composition has the correct osmolarity so that it will have the desired tonicity with respect to the cells that are being exposed to the composition.

Applicant argues that there is no motivation to choose the iodide agents as the tonicity agents taught by Banerjee et al. This argument is not persuasive. The agents listed by Banerjee et al. are conventional tonicity adjusting agents, wherein each of the listed agents is equivalent in its effects.

Applicant argues, "such combination would not suggest the use of an iodide tonicity adjusting agent in an amount sufficient to 'stabilize the composition against degradation thus maintaining high radiochemical purity of the composition". This argument is not persuasive, as it is not commensurate in scope with the instant claims, which do not recite any amounts.

Applicant argues, "Bannerjee obviously teaches nothing about the stabilizing effect of iodide in a radiopharmaceutical, as discovered by applicants". This argument is not persuasive. A compound and its properties are inseparable. Thus, while the combination of reference does not explicitly state this property, it is a characteristic of the composition of the combined references.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is 571-272-0634. The examiner can normally be reached on M&R (5:30-4).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

lqw

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